

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C. 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 25 July 2000 (25.07.00)	
International application No. PCT/US99/27365	Applicant's or agent's file reference 2444-107.PCT
International filing date (day/month/year) 19 November 1999 (19.11.99)	Priority date (day/month/year) 19 November 1998 (19.11.98)
Applicant CHANG, Esther, H. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
16 June 2000 (16.06.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Zakaria EL KHODARY

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

SAXE, Stephen, A.
Rothwell, Figg, Ernst & Kurz
Suite 701 East
Columbia Square
555 13th Street N.W.
Washington, DC 20004
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 08 August 2001 (08.08.01)	Applicant's or agent's file reference 2444-107.PCT
International application No. PCT/US99/27365	International filing date (day/month/year) 19 November 1999 (19.11.99)

IMPORTANT NOTIFICATION

1. The following indications appeared on record concerning:

☒ the applicant
 ☒ the inventor
 ☐ the agent
 ☐ the common representative

Name and Address

PIROLLO, Kathleen
547 Anderson Avenue
Rockville, MA 20850
United States of America

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person
 ☐ the name
 ☒ the address
 ☐ the nationality
 ☐ the residence

Name and Address

PIROLLO, Kathleen
547 Anderson Avenue
Rockville, MD 20850
United States of America

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office
 ☐ the designated Offices concerned
☐ the International Searching Authority
 ☒ the elected Offices concerned
☐ the International Preliminary Examining Authority
 ☐ other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

V. Gross (Fax 338.87.40)

Telephone No.: (41-22) 338.83.38

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 2444-107.PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 99/ 27365	International filing date (day/month/year) 19/11/1999	(Earliest) Priority Date (day/month/year) 19/11/1998
Applicant GEORGETOWN UNIVERSITY et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 1-32 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/86 C12N15/87 A61K48/00 A61K47/48 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 38723 A (BARBER JACK ; IMMUSOL INC (US); LI QI XIANG (US); YU GANG (US); YU) 23 October 1997 (1997-10-23) abstract; claims 1-3,8,9,27,29 page 1, line 15 - line 23 page 3, line 2 - line 22 page 11, line 1 - line 6 page 58, line 22 - line 29 ---	1-32
X	WO 98 40508 A (SOSNOWSKI (US)) 17 September 1998 (1998-09-17) abstract; claims 1,3,4,6,9,31 page 4, line 17 -page 5, line 7 page 7, line 11 - line 25 page 27, line 14 -page 29, line 26 page 34, line 21 -page 35, line 22 page 93, line 12 - line 26 --- -/--	1-6,8-32

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

27 April 2000

Date of mailing of the international search report

08/05/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

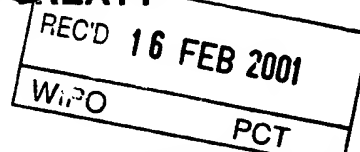
Niemann, F

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MILLER N ET AL: "TARGETED VECTORS FOR GENE THERAPY" FASEB JOURNAL,US,FED. OF AMERICAN SOC. FOR EXPERIMENTAL BIOLOGY, BETHESDA, MD, vol. 9, no. 2, 1 February 1995 (1995-02-01), pages 190-199, XP000616414 ISSN: 0892-6638 page 192, right-hand column, line 14 - line 52 page 194, right-hand column, line 8 -page 195, left-hand column, line 35 ---	1-6,8-32
A	DEONARAIN M P: "LIGAND-TARGETED RECEPTOR-MEDIATED VECTORS FOR GENE DELIVERY" EXPERT OPINION ON THERAPEUTIC PATENTS,GB,ASHLEY PUBLICATIONS, vol. 8, no. 1, January 1998 (1998-01), pages 53-69, XP002910260 ISSN: 1354-3776 table 1 ---	9-12
A	WO 94 24299 A (COTTEN MATTHEW ;WAGNER ERNST (AT); BOEHRINGER INGELHEIM INT (DE);) 27 October 1994 (1994-10-27) cited in the application abstract; figure 1 page 6, line 34 -page 7, line 23 figure 1 ---	1-6, 12-16, 19-32
A	XU L ET AL: "Transferrin-liposome-mediated p53 sensitization of squamous cell carcinoma of the head and neck to radiation in vitro" HUMAN GENE THERAPY,XX,XX, vol. 8, no. 4, 1 March 1997 (1997-03-01), pages 467-475-475, XP002098089 ISSN: 1043-0342 abstract page 468, right-hand column, line 16 - line 40 -----	17-32



Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9738723	A	23-10-1997	AU 2678097 A CA 2251738 A EP 0927044 A	07-11-1997 23-10-1997 07-07-1999
WO 9840508	A	17-09-1998	AU 6462998 A EP 0973926 A	29-09-1998 26-01-2000
WO 9424299	A	27-10-1994	DE 4311651 A EP 0694071 A JP 8508648 T US 5693509 A	13-10-1994 31-01-1996 17-09-1996 02-12-1997

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2444-107.PCT		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/27365	International filing date (day/month/year) 19/11/1999	Priority date (day/month/year) 19/11/1998	
International Patent Classification (IPC) or national classification and IPC C12N15/86			
Applicant GEORGETOWN UNIVERSITY et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application 			
Date of submission of the demand 16/06/2000		Date of completion of this report 13.02.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Grosskopf, R Telephone No. +49 89 2399 8714 	

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US99/27365

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

Description, pages:

1-27 as originally filed

Claims, No.:

1-32 as originally filed

Drawings, sheets:

1-7 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US99/27365

☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

see separate sheet

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-11,13-25,27-29,31-32.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 1-11,13-25,27-29,31-33 are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims 1-32

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US99/27365

	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-32
Industrial applicability (IA)	Yes:	Claims	1-18
	No:	Claims	19-32 (no opinion)

2. Citations and explanations
see separate sheet

Ad item I:

The amendments made in the claims cannot be taken into account.

This is due to the fact that there is no explicit support for the expression "bound directly". It appears as if, according to the Applicant, a support can be found, implicitly, in the methods described in the example. However, in this context it must be mentioned that the description or the examples do not make any statements with regard to the nature of binding and/or do not explain what should be meant by a "direct" binding. Finally, in the context of the claims and when considered in the light of the prior art, said term is unclear.

Ad item III:

The present application relates to the delivery of viruses into cell, said viruses being "combined" with a cell targeting ligand without covalent linkage.

Said procedure should lead to better results when compared with the prior art wherein the targeting ligands are covalently bound to the viruses.

The **only** combination for which any experimental results have been shown in the present application relates to a combination of transferrin with adenovirus.

Thus, with the exception of Claims 12, 26 and 30, all other claims which comprise an undue generalisation of one or both of the essential compounds must be considered as being not sufficiently supported by the description since no confirmation for the alleged results is given with respect to any of all other possible combinations.

Ad item V:

As indicated above, in principle, the claims are not supported over the whole breadth claimed.

Moreover, the vague wording of the general claims, does not allow a distinction from e.g. D1 (WO 98/40508), wherein viruses are non-covalently bound to bispecific antibodies or fusions of ligands with parts of antibodies (see e.g. page 26 of D1).

Both the bispecific antibodies and the fusion proteins may be considered as being cell-targeting ligands which are bound to the virus. In view of the fact that,

although comprising two functional "domains", said antibodies or fusion proteins form a single entity.

Thus, a distinction between Claim 1 (and the other general claims; see especially Claim 9) and D1 is not possible (regardless whether read with or without the expression "bound directly").

Claim 12 **relates** to a "vector" which comprises a virus and transferrin, said transferrin not being covalently bound to the vector.

At least in its present form said claim does not seem to be inventive (or novel) since the prior art includes the use of transferrin for the delivery of nucleic acids or viruses into a cell. Since Claim 12 does not exclude the possibility that the transferrin is "indirectly" bound to the viruses the "compositions" and methods of the art seem to fall within the scope of Claim 12, 26 and 30 (see e.g. D2; MILLER N ET AL: "TARGETED VECTORS FOR GENE THERAPY" FASEB JOURNAL, US, FED. OF AMERICAN SOC. FOR EXPERIMENTAL BIOLOGY, BETHESDA, MD, vol. 9, no. 2, 1 February 1995 (1995-02-01), pages 190-199, XP000616414 ISSN: 0892-6638).

Finally, it should be mentioned that comparative results should be made with regard to viruses wherein the transferrin is (non-covalently) bound via a linker to the virus but not with regard to the naked virus.

For the assessment of the present claims 19 to 32 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.